

REMARKS

Entry of the present amendment and reconsideration of the claims is requested. The present amendment should be entered since it places the claims in condition for allowance or, alternatively, in better condition for appeal. Claims 1-2, 14-15, 28, 30, 34 and 35 are pending in the instant application. Each amended claim has written support in the application; accordingly, no new matter has been added to the application.

Claim Objections

The Examiner's objection to claims 26-27 has been mooted by cancellation of those claims.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner's rejections of claim 16, 21-23 and 29 for indefiniteness have been rendered moot by Applicants' cancellation of those claims. The remaining indefiniteness rejections are discussed below.

Claims 1 and 15 stand rejected as allegedly being indefinite because the particular solvent in which the claimed polypeptides are soluble is not specified. Claims 1 and 15 have been amended to specify that the claimed polypeptides must be soluble "in 25 mM Hepes-potassium hydroxide, pH 7.5, 0.15M potassium chloride, 1 mM EDTA, 0.03% sodium azide and 5 m DTT buffer." Of course, the scope of the claims includes polypeptides which are also soluble in other solvents. Specific support for this amendment can be found in the specification at page 46, lines 3-6. The indefiniteness rejection of these claims should be withdrawn. Such action is requested.

Claim 30 also stands rejected as indefinite. According to the Examiner, it is unclear whether the phrase “characterized by the structural coordinates...” is intended to be directed to “the polypeptide of the crystal of claim 28 or the crystal itself.” Claim 30 no longer refers to structural coordinates; however, dependent claims 34 and 35 do make this reference. As suggested by the examiner, the coordinates refer to the spatial, 3-dimensional arrangement of the atoms of the polypeptide and the $\text{Ac-}^{6\text{Cl}}\text{WAC}_3\text{cE}$ molecule. The wording of new claims 34 and 35 should make this point clear. Rejection of new claims 34 and 35 for indefiniteness would not be proper. Withdrawal of the rejection is requested.

Rejections under 35 U.S.C. § 112, First Paragraph – Written Description/New Matter

Claims 1-2, 15-17, 21-23 and 26-30 stand rejected for an alleged lack of adequate written description. In view of Applicants’ cancellation of claims 16-17, 21-23, 26 and 29, the rejection of these claims is moot. The remaining written description rejections are addressed below.

The Examiner has rejected claim 1 for lack of written description/new matter. The examiner took the position that the specification only provides written support for an HDM2 (F55Y/Y76H) polypeptide complex that is soluble at 34 mg/ml concentration but not any polypeptide of SEQ ID NO: 4. Thus, the examiner states, the amendment to claim 1 submitted in the Feb. 24, 2006 Amendment and Response adds new matter to the application. Applicants disagree. The interpretation of the specification being espoused by the examiner is overly narrow and literal. The specification clearly supports the elements added to claim 1.

The specification makes the following blanket statement at page 79, lines 1-5:

The present invention is not to be limited in scope by the specific embodiments describe herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims.

This passage clearly describes the Applicant's intent not to limit the scope of possible embodiments of the present invention to those specifically and literally described. Rather, the specification was intended to be interpreted broadly and liberally with respect to the scope of the invention.

The specification clearly states that an object of the invention is to create HDM2 polypeptides which are highly soluble at high concentrations. See, for example, page 3, lines 30-32:

Thus, there is a need to obtain nucleic acids that encode an Hdm2 protein that is soluble and stable at high protein concentrations even when the protein is free of p53 or fragments thereof.

See also page 4, lines 11-15:

The present invention provides modified Hdm2 proteins that are amenable to crystallization and are soluble in E. coli extracts. The present invention further discloses a set of amino acid substitutions of the Hdm2 protein that improve its solubility and/or stability without compromising its ability to bind p53.

HDM2 protein is not defined or described as narrowly as the examiner is assuming. The term includes any of the polypeptides of SEQ ID NO: 4. There is nothing in the specification that indicated otherwise. For example, the specification states the following at page 12, lines 5-14 :

As used herein a “modified Hdm2” is identical to the wild-type Hdm2(17-125) except it has at least one amino acid substitution, i.e., it has one or more amino acid substitutions. Furthermore, a modified Hmd2 of the present invention comprises an amino acid substitution at one or more of the seven positions listed in Table 1 and denoted in SEQ ID NO: 4. Preferably, that amino acid substitution is one that is specifically defined in Table 1 (and denoted in SEQ ID NO: 4).

The 34 mg/ml concentration value is found in example 2 in relation to the concentration of HDM2 (F55Y/Y76H). This value was intended to describe a single, specific concentration at which HDM2 (F55Y/Y76H) and other similar HDM2 proteins are soluble. As stated in the passage on page 79, the invention should not be limited to specifically described embodiments. Indeed, a practitioner of ordinary skill in the art would have appreciated that similar polypeptides would also be soluble at this concentration.

It should be clear, *e.g.*, in view of the above-referenced passages, that applicants contemplated HDM2 polypeptides that are soluble in a wide range of high concentrations. The 34 mg/ml value is but a single example of such values and the scope of the invention should by no means be interpreted to be limited to HDM2 (F55Y/Y76H) at this concentration. The new matter rejection is improper and its withdrawal is requested.

Claims 28 and 30 also stand rejected for lack of written description. Specifically, the Examiner has maintained that the specification fails to sufficiently describe a genus of crystals covered by the claims.

Amended claims 28 and 30 describe the claimed crystals by amino acid sequence (respecting the polypeptide), structure (respecting the tripeptide), space group and unit cell dimensions. Thus, the claimed crystals are thoroughly described and compliant with the written description requirement. Indeed, the

examiner implied that such claims would be compliant in the August 26, 2005 office action (page 8). Withdrawal of the claim rejections on written description grounds is requested.

Rejections under 35 U.S.C. § 112, First Paragraph - Enablement

Claims 16-17, 21-23, and 26-30 stand rejected for lack of enablement. As discussed above, Applicants have cancelled claims 16-17, 21-23, 26-27 and 29, and have amended claims 28 and 30 to describe crystals which are clearly exemplified in the present specification. For example, examples 1-3 describe how to generate and crystallize the HDM2 polypeptides. Structural characteristics of the claimed crystals are set forth in the tables at page 46, lines 16-25 and at page 63, lines 23-33. Applicants respectfully request withdrawal of the enablement rejections in view of the amended claims.

CONCLUSION

The claims are in condition for allowance. Such action is requested. If the undersigned can be of assistance in advancing the application to allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,

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